Mouse behavior on ISS: The emergence of distinctive, organized group circling behavior unique to spaceflight

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Background

- As interest in long duration space habitation increases, understanding behavioral phenotypes of model organisms living within habitats engineered to fly them is vital for <u>*designing*</u>, <u>*validating*</u>, and <u>*interpreting*</u> spaceflight studies

- Why study behavior in space?
  - Direct knowledge of how an organism interacts with its environment is imperative for ensuring the biocompatibility of spaceflight habitats in the weightlessness space environment
  - Behavior represents the integrated biology of the whole animal
  - Detailed information on forms, levels and patterning of behavior provide important insights into neural and physiological function
  - Understanding how long it takes for organisms to acclimate to living in space and how successfully they adapt to the space environment
  - Vital for interpreting experimental endpoints influenced by physical activity, feeding and drinking, social interactions, and other behavioral actions
  - The ability to translate research findings, thereby informing human health in space requires direct observation to establish confidence that behavior is not changed in ways that confound experimental outcomes

Background

- Few published reports of rodent behavior in-flight
  - NASA Space Shuttle (*9 and 11 days*) - Ronca, Fritzsch, Bruce & Alberts, *Behavioral Neuroscience, 122(1), 224-232, 2008*
  - Italian Mouse Drawer System (*90 days*) - Cancedda, Liu, Ruggiu, Tavella, Biticchi, Santucci, Schwartz, Ciparelli, Falcetti, Tenconi, Cotronel, & Pignataro, *PLoS ONE 7(5): e32243, 2012*
  - Russian BION M1 (*30 days*) - Andreev-Andrievskiy, Popova, Boyle, Vinogradova, Nemirovskaya, Alberts, Soldatov, Shenkman, Dolgov, Ilyin, Anokhin, Tsvirkun, & Sychev, *PLoS ONE 9(8): e104830, 2013*

- This Project
  - Rodent Research Hardware and Operations Validation (Rodent Research-1) Mission launched on Sept 21, 2014 in an unmanned Dragon Capsule (Space-X4)
  - Establish biocompatibility of mice housed within the NASA Rodent Habitat (RH) in flight
  - Utilized video images originally acquired for daily health evaluations to conduct a retrospective analysis of mouse behavior in-flight
  - Major findings:
    - ✓ Comparable forms/levels of species-typical behaviors in NASA Spaceflight and Ground Control
    - ✓ Spaceflight mice were more active that Ground Controls
    - ✓ Emergence of a novel group circling or ‘race-tracking’ behavior unique to the NASA spaceflight mice

Methods

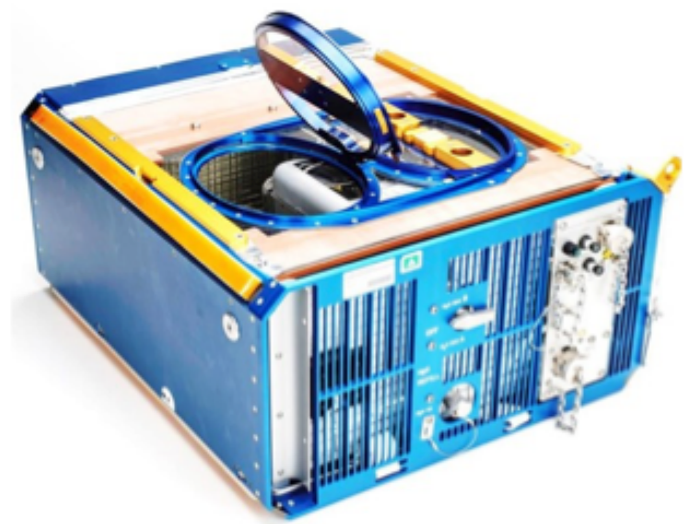
- Ten C57BL/6J female mice, 16 weeks old at launch, were flown
- Beginning on L-21, mice were pre-adapted to NASA Rodent Food Bars and deionized, autoclaved water via lixit spouts
- Food and water available *ad libitum*
- Mice were maintained on a 12:12hr dark/light cycle (0600-1800 GMT, lights on)
- On L–6, mice were weight-matched and assigned to either Flight, Identically Housed Ground Control, Vivarium Ground Control or Basal conditions (n=10/group)*

**Video acquired from Flight and Identically-Housed Ground Control groups only*

Methods

- On L+0, the ten NASA mice, assigned to two cohorts of five housed in a bisected Rodent Habitat transporter unit, were launched in an unmanned Dragon Capsule (SpaceX4) from Kennedy Space Center (KSC) to the International Space Station (ISS)
- On L+4, Flt mice were transferred to ISS RH units
- Daily videography was initiated on L+5

Rodent Habitat

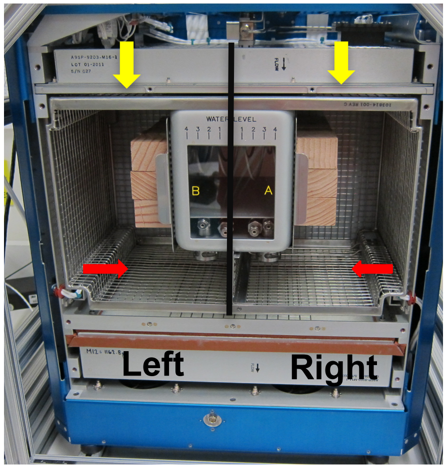


- FLT and GC mice were treated identically except for exposure to launch and spaceflight
- GC mice were housed in the ISS Environmental Simulator at KSC where environmental parameters (temperature, relative humidity, and CO_2) were simulated with a 4-day delay relative to FLT mice

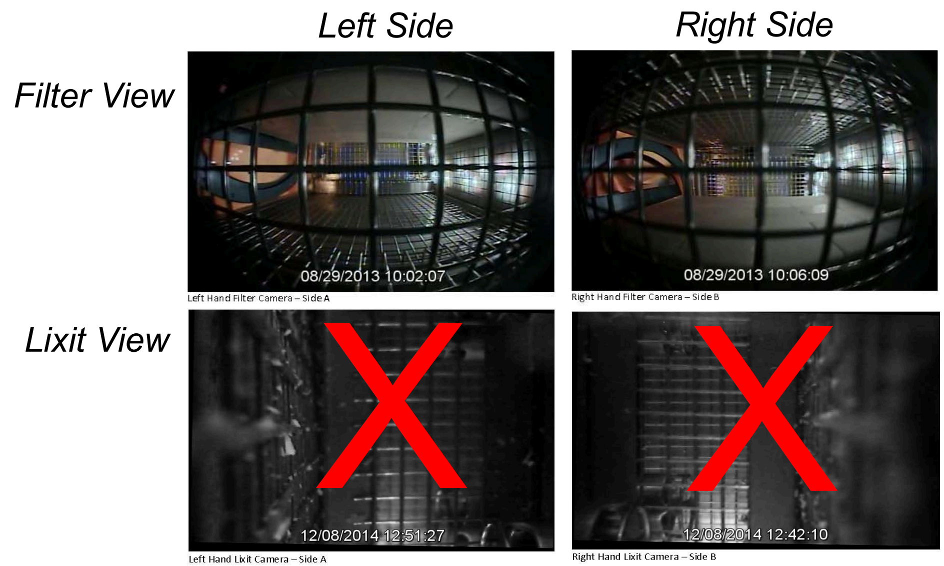
Dual Housing Areas with Designated Camera Positions

Filter Cameras

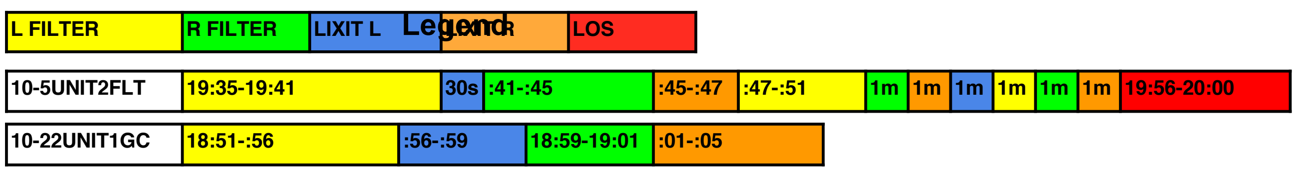
Lixit Cameras



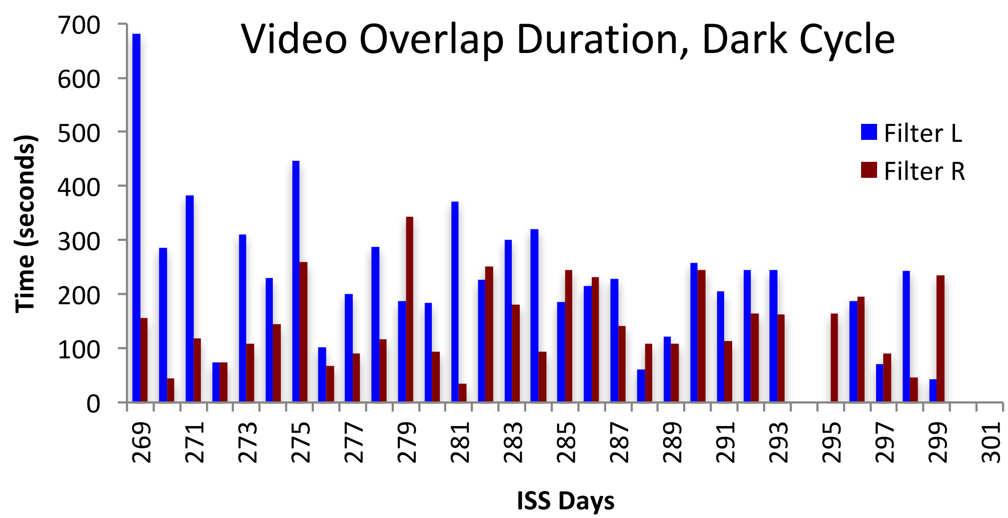
Camera Views



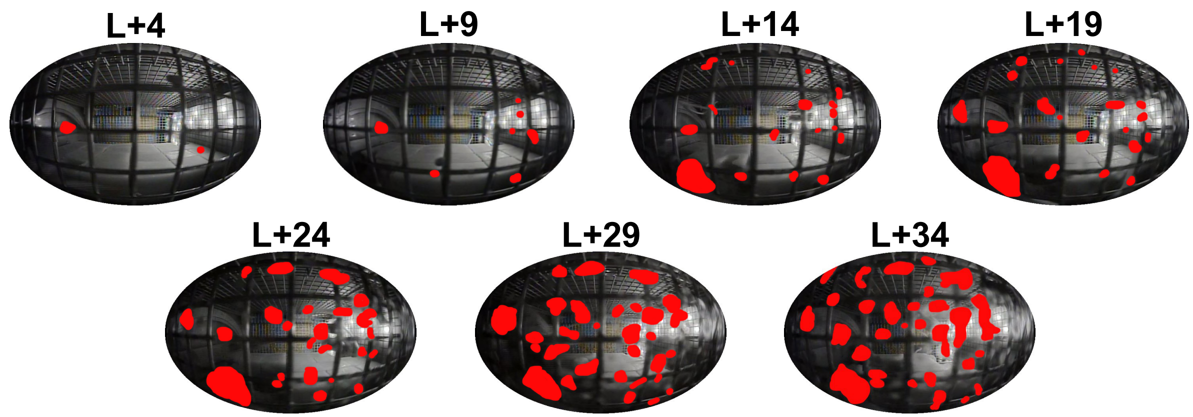
Sample Video Segments

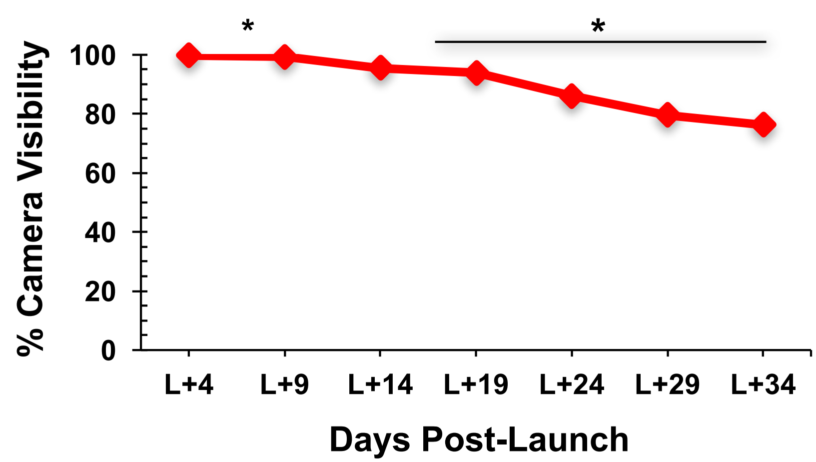


- *RR1 images were collected at varying durations across camera views and days (largely dark cycle)*
- *Catalogued video segments across 33 mission days then analyzed overlap, allowing for a 1-hr window across FLT, GC and L,R habitat sides*



Camera Visibility Over Time



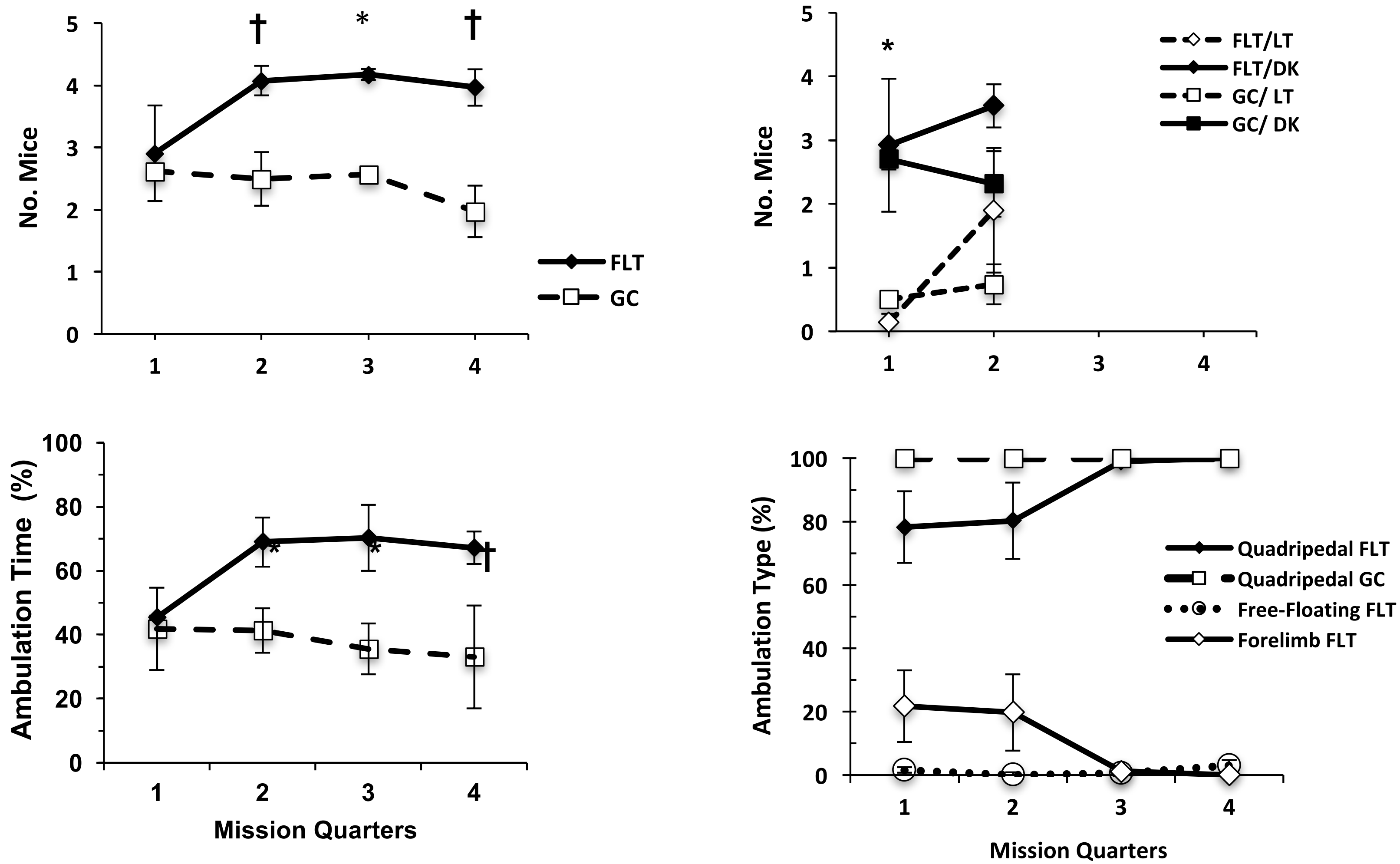


NASA RR1 VIDEO HERE

SKYLAB VIDEO HERE

https://www.youtube.com/watch?v=dmnmuTv4pGE

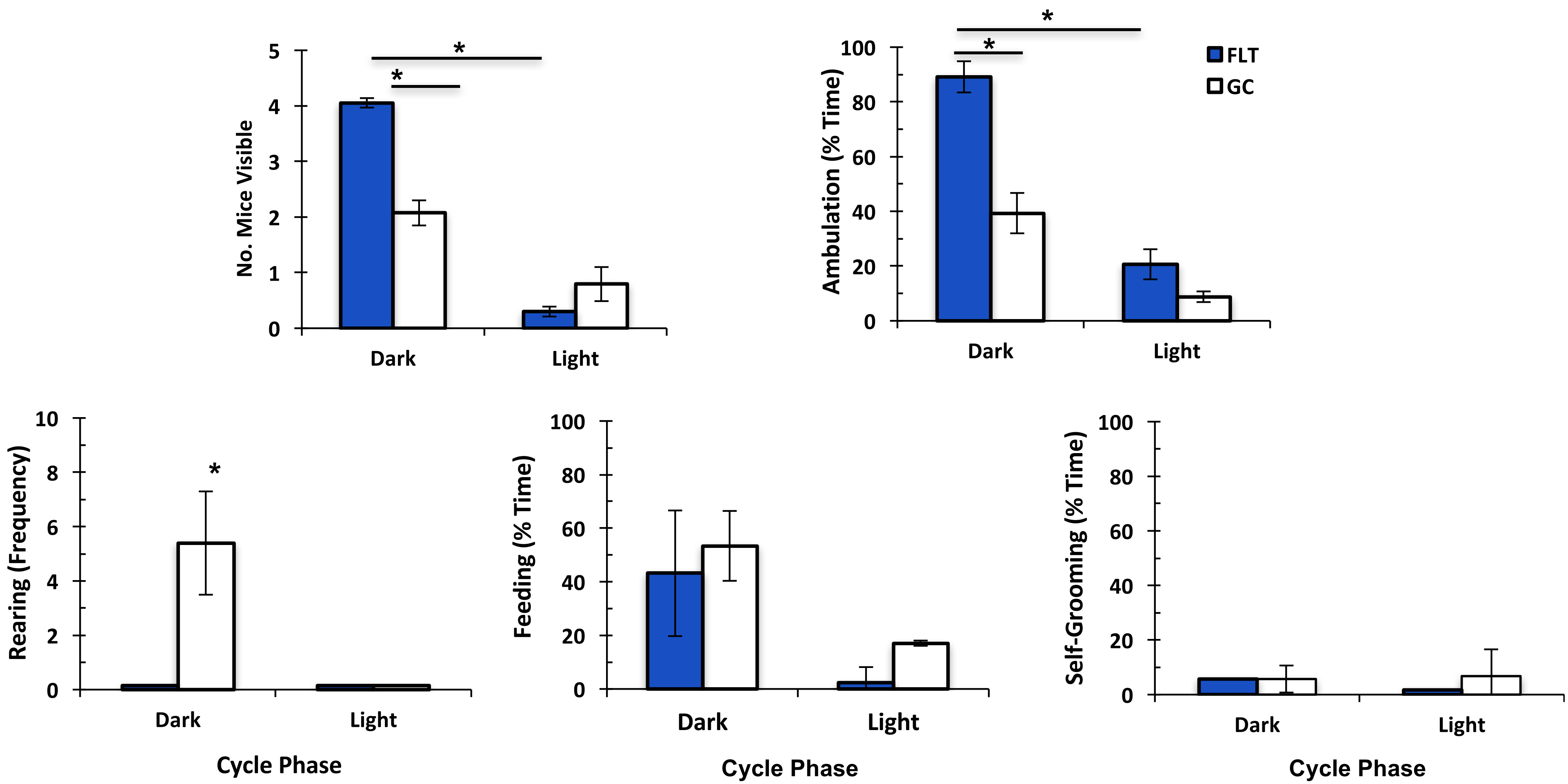
Mission Long Analysis (L+ 4 to L+34)



✓ Spaceflight and Ground Control Mice:

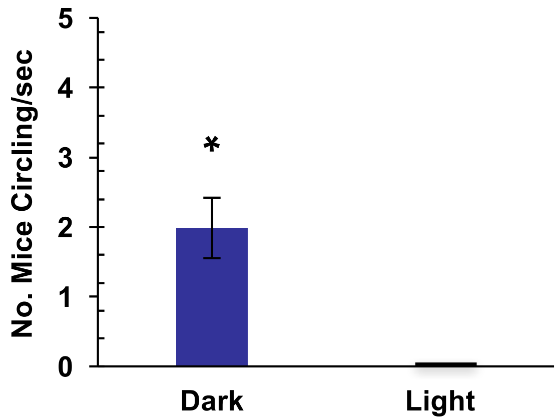
- Spent comparable amounts of time feeding and self-grooming
- Rarely exhibited affiliative (huddling, allo-grooming) or antagonistic (tail-pulling, biting) behaviors

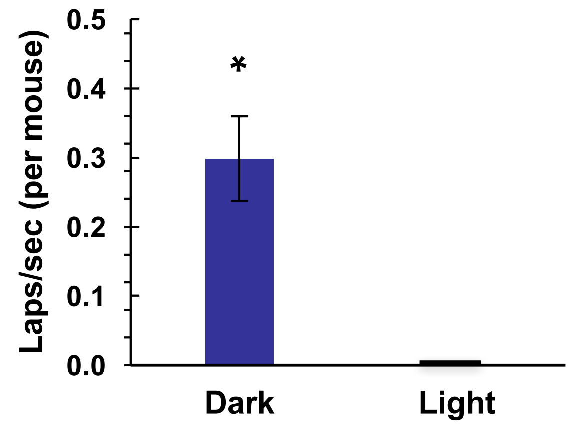
Circadian Analysis (L+29)

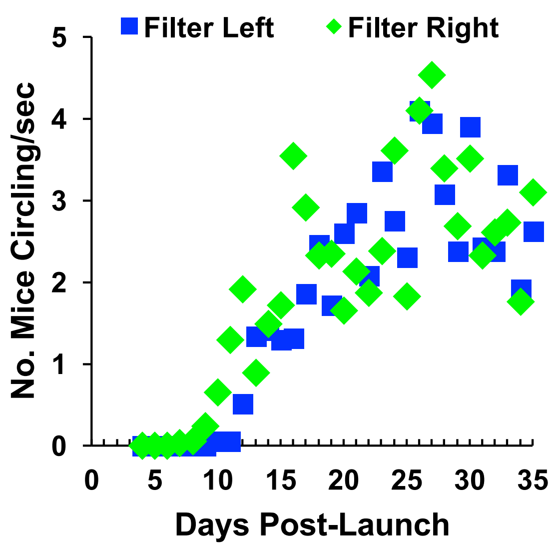


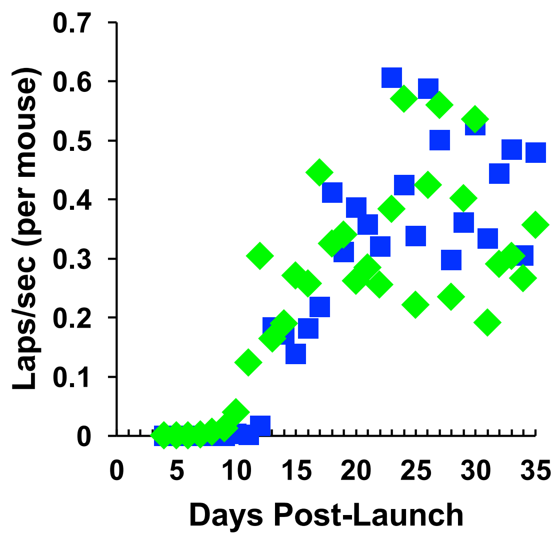
Circling Analysis

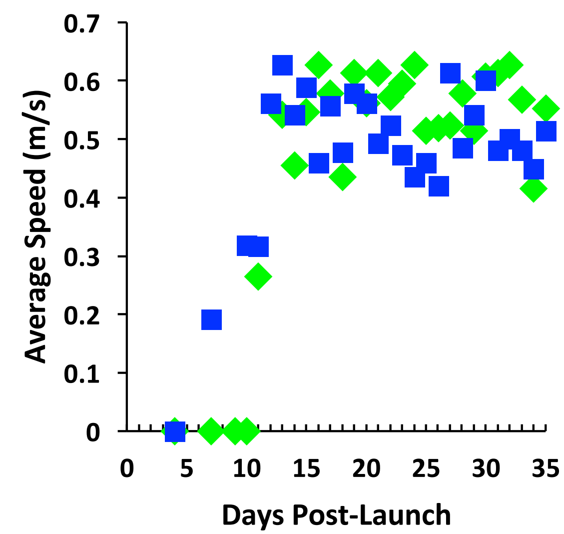
Behavior Observed	Day First Observed	
	Left Filter	Right Filter
Flipping	L+9	L+7
Circling	L+10	L+7
Multi-Circling	L+10	L+8
Group Multi-Circling	L+12	L+10





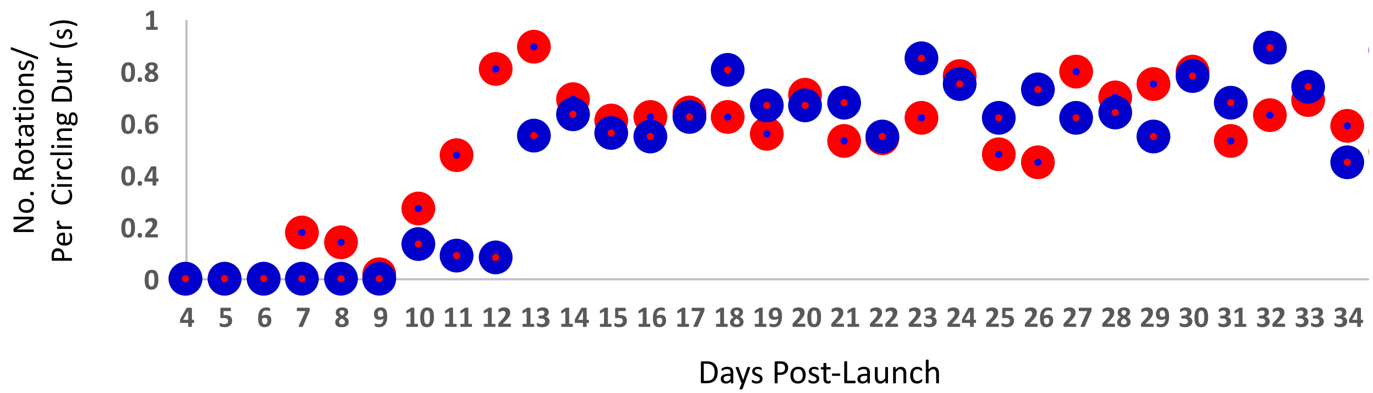




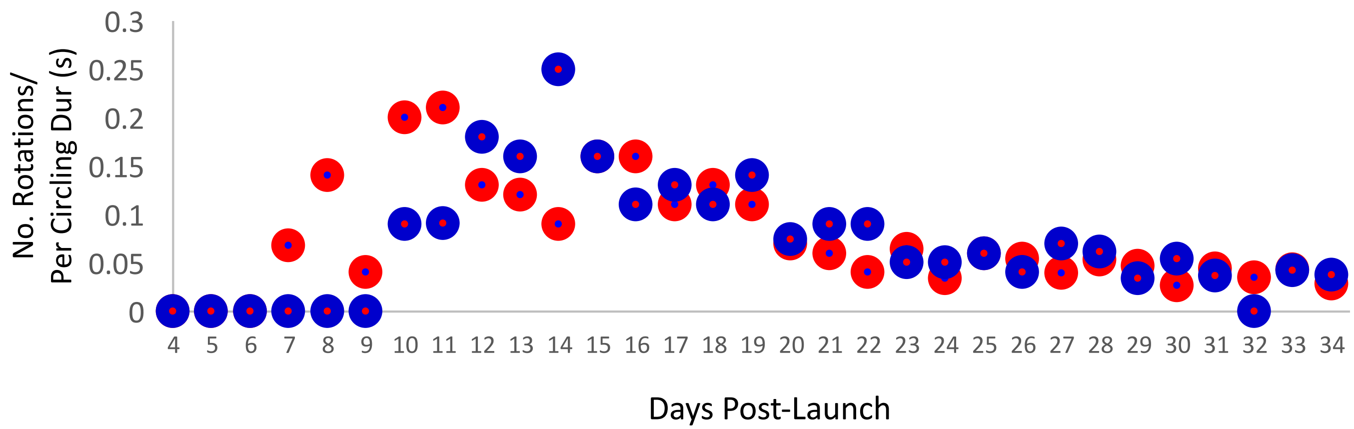


Group Circling Analysis

No. Complete Rotations



Collisions



Summary of Findings

- Modest decline in visibility (~20%) over mission duration
- Mission-Long Analyses revealed increased presence of spaceflight mice in the larger Filter area of the habitat and greater amounts of time spent ambulating
- Comparable forms and levels of species typical behaviors- feeding, self-grooming, and rare occurrence of affiliative and antagonistic behaviors
- Late mission around-the-clock video samples provided evidence that circadian timing was intact
- Circling behavior emerged in both mouse cohorts according to a common timetable and progression of individual and group milestones
- Group circling achieved an astoundingly high level of organization as evidenced by increasing numbers and durations of complete rotations with a concomitant decrease in collisions
- RR1 limitations, although highly detailed behavioral analysis was still possible:
    - Lack of individual mouse identifiers
    - Behaviors performed within the Lixit area, such as drinking (and possibly huddling and other social behaviors)
    - Limited light cycle video images

Interpretations and Conclusions

- Possible explanations for circling behavior
  - Stress-Induced Motor Stereotypy
  - Boredom/Rewarding Value of Physical Exercise
  - Vestibular: Space Motion Sickness, Self-Stimulation
  - Social Stimulation?

- Evidence does not support the view that circling occurred as a stress-induced stereotypy
  - Behavioral indices of stress, *viz.,* antagonistic behaviors such as biting and tail-pulling, were rarely observed, and barbering never observed, in spaceflight mice
  - Physiological signs of stress were not observed- measures comparable in flight and control mice
    - Body weight gain, feeding, drinking, grooming and fur condition during flight
    - Postmortem adrenal and thymus weights analyses

- Our findings demonstrate that mouse circling behavior in space was highly organized, showing clear features of increased individual, then group organization
  - Circling behavior in space clearly represents a unique, coordinated group activity not observed at 1g

- Collectively, our observations do suggest that stress was a not likely a major driver of mouse circling in space but rather, suggest a form of self-generated environmental enrichment

- Circling in space could have unanticipated effects on certain experimental endpoints including altered blood flow, muscle use, metabolic and other effects. Efforts are underway to determine whether environmental enrichment can potentially reduce circling behavior in space.

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